Annals of Clinical and Analytical Medicine
Original Research

Effects of hypothyroidism and hyperthyroidism on hematological and biochemical parameters

Hypothyroidism and hyperthyroidism

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Abstract
Aim: This study aimed to compare the hematological and biochemical parameters of hypothyroid and hyperthyroid patients when they were first diagnosed.
Material and Methods: This study is a retrospective cross-sectional study. Hyperthyroid patients were diagnosed with elevated serum levels of fT3 and/or fT4 but decreased TSH levels compared to reference ranges (fT4: 12.3-20.2 pmol/L; fT3: 3.71–6.70 pmol/L; and TSH, 0.30–3.94 mIU/L). Hypothyroid patients were diagnosed with decreased serum levels of fT3 and/or fT4 but elevated serum levels of TSH.
Results: A total of 727 patients, 349 (277F/72M) diagnosed with hypothyroidism and 378 (306F/72M) diagnosed with hyperthyroidism, were included in this study. The number of women was statistically significantly higher ($p<0.01$) than men in both hypothyroid (%79) and hyperthyroid (%80) patient groups. When we compared the hypothyroidism and hyperthyroidism groups, we found a statistically significant difference between groups in terms of TSH, fT3, fT4, MPV, PLT, urea, creatinine, LDL-C, TC, TG, and TG/HDL-C ratio. In this study, a significant increase ($p<0.01$) in serum levels of TG, TC and LDL-C was observed in hypothyroid patients compared to hyperthyroid patients. We also found a negative significant correlation between fT3 and LDL-C in patients with hyperthyroidism ($r: - 0.238$, $p<0.01$). Moreover, vitamin B12 deficiency (B12 levels <175 pg\ml), was present in 8% of hypothyroid patients and 6.3% of hyperthyroid patients.
Discussion: Our findings emphasize that it is important to follow up both hypothyroid and hyperthyroid patients in terms of lipid parameters. Especially in patients with hypothyroidism, lipid metabolism is highly affected.

Keywords
Hyperthyroidism, Hypothyroidism, Lipid Metabolism, TG/HDL-C Ratio

DOI: 10.4328/ACAM.21554 Received: 2022-12-19 Accepted: 2023-02-02 Published Online: 2023-02-22 Printed: 2023-03-25 Ann Clin Anal Med 2023;14(Suppl 1):S10-14
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This study was approved by the Ethics Committee of KTO Karatay University (Date: 2022-05-23, No: 2022/012-05)

Introduction

Thyroid hormones are hormones that affect all systems in the body, and all cells are also targets of thyroid hormones. It has effects on almost all metabolic pathways, especially carbohydrate, protein and lipid metabolism. Two main hormones are synthesized and released from the thyroid gland. These are thyroxine (fT4) and triiodothyronine (fT3). fT4 is a prohormone and is present in higher concentrations than fT3 [1,2]. Triiodothyronine is a biologically active thyroid hormone. There is an inverse relationship between serum thyroid hormones and Thyroid Stimulating Hormone (TSH). Even very small changes in hormones cause big fluctuations in TSH levels [2,3].

Thyroid gland diseases are among the most common endocrine disorders in the world and are second only to diabetes.

These diseases are characterized by abnormal circulating thyroid hormones and TSH levels [2,4]. Hypothyroidism is a disease that occurs with thyroid hormone deficiency or ineffectiveness at the cellular tissue level and progresses with a slowdown in metabolic events. There are classifications of primary, secondary, tertiary, overt and subclinical hypothyroidism. Hypothyroidism may be overt with high TSH and low fT4 levels, or subclinical with a normal fT4 level despite a high TSH level [5,6]. Its prevalence in the community is between 4-5%. 0.8% of women and 0.3% of men have overt hypothyroidism [7].

Hypothyroidism is closely related to increased serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG), as thyroid hormones play a role in the activity of important enzymes in the pathway of cholesterol production and conversion [5,8]. Patients with thyroid dysfunction are likely to have a high incidence of insulin resistance, type 2 diabetes, and cardiovascular disease [9]. Abnormalities in lipid profiles in patients with overt hypothyroidism are well-defined. A study at the Mayo Clinic noted abnormalities in more than 90% of 295 patients with overt hypothyroidism [10].

Hyperthyroidism is a disease that occurs when the thyroid gland is overactive, that is, it produces too much thyroid hormone. Although there are many causes of hyperthyroidism, its frequency is affected by dietary iodine intake, and some cases are due to autoimmune (graves' disease) disease [11]. While subclinical (normal fT3, fT4 with suppressed TSH) hyperthyroidism is more common in women over 65 years of age than men, overt (high fT3, fT4 with suppressed TSH) hyperthyroidism rates are 0.4 per 1000 women and 0.1 per 1000 men, and the prevalence varies according to age [11,12].

In contrast to hypothyroidism, signs and symptoms of high thyroid hormone exposure to peripheral tissues in hyperthyroidism reflect a hypermetabolic state. A hyperthyroid patient may classically show symptoms such as palpitations, weight loss, irritability, sweating, increased bowel movements, osteoporosis, menstrual irregularity, etc., due to this increased metabolic activity state [12].

In light of this information, we aimed to compare the hematology and biochemistry parameters of hypothyroid and hyperthyroid patients when they were first diagnosed. In the literature, there are studies evaluating the laboratory parameters separately in hypothyroid and hyperthyroid patients. However, as in our study, there is no study comparing both groups in terms of both hematological and biochemical parameters.

Material and Methods

Study population

This study is a retrospective cross-sectional study. After the approval of the ethics committee, patients diagnosed with hypothyroidism and hyperthyroidism in the Department of Internal Medicine of the Van Training and Research Hospital of Health Sciences University Between June 1, 2012 and June 1, 2022 were retrospectively analyzed. A total of 727 (diagnosed with hypothyroidism: 349, diagnosed with hyperthyroidism: 378) patients were included in the study.

The diagnosis of hypothyroidism and hyperthyroidism were made according to the guidelines (available at: https://temd.org.tr/yayinlar/kilavuzlar). Hyperthyroid patients were diagnosed with elevated serum levels of fT3 and/or fT4 but decreased TSH levels compared to reference ranges. Hypothyroid patients were diagnosed with decreased serum levels of fT3 and/or fT4 but elevated serum levels of TSH (reference ranges: fT4: 12.3-20.2 pmol/L; fT3: 3.71–6.70 pmol/L; and TSH: 0.30–3.94 mIU/L). The inclusion criteria for the study were: age 18- 65 years (men, non-pregnant women), newly diagnosed and untreated patients with hypothyroidism or hyperthyroidism, without other additional disease diagnosis in the system, and having hematological and biochemical parameters results.

The exclusion criteria for the study were: age <18 years >65, pregnant women, patients with diabetes mellitus, hypertension, chronic inflammatory disease etc., patients with missing data on hematological and biochemical parameters.

Age, gender, hematological and biochemical parameters data of the patients were obtained retrospectively from the hospital automation system and patient files. The triglyceride-high-density lipoprotein (HDL-C) ratio (TG/HDL) values were calculated by dividing the TG result by the HDL-C result in the biochemistry results. The obtained data were saved in Excel, and statistical analysis was performed.

Statistical analysis

Statistical analysis of the data was performed using the SPSS 27.0 package program (IBM SPSS, Chicago, IL, USA). The conformity of the data to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). In the evaluation of numerical data, arithmetic mean, standard deviation, median (1st quartile-3rd quarter), minimum and maximum values were used. Frequency distributions and percentages were used to summarize categorical data. The Chi-square (x2) test was used to compare categorical data. Comparison of non-normally distributed numerical data with categorical data was done with the Man-Whitney U test. Correlations of non-normally distributed numerical variables were analyzed with the Spearman correlation coefficient. Cases were considered statistically significant when p was less than 0.05.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

A total of 727 patients, 349 (277F/72M) diagnosed with hypothyroidism and 378 (306F/72M) diagnosed with hyperthyroidism, were included in this study. The median age

of all patients was 47±14.48 years. The number of women was statistically significantly higher (p<0.01) than men in both hypothyroid (%79) and hyperthyroid (%80) patient groups. There were no statistically significant differences between the hypothyroid and hyperthyroid groups when compared with the Chi-square test in terms of gender (p: 0.59).

When the laboratory parameters of females and males in the hypothyroid group were compared, we found statistically significantly higher levels of platelets (PLT), TC and HDL-C in females compared to males. In males, HGB, AST, ALT, urea, creatinine, Fe, ferritin were statistically significantly higher than in females. In the hypothyroid group, there was no statistically significant difference between men and women in terms of age, thyroid function tests, vitamin D, vitamin B12, HbA1c, LDL-C (p>0.05).

When laboratory parameters of females and males in the hyperthyroid group were compared, we found statistically significantly higher levels of PLT, TC, HDL-C, LDL-C in females compared to males. In males, HGB, MPV, AST, ALT, urea, creatinine, ferritin, vitamin D, TG and TG/HDL-C ratio were statistically significantly higher than in females. In the hyperthyroid group, we found that the fT3 and fT4 levels were significantly lower in females than in males. In the hyperthyroid group, there was no statistically significant difference between men and women in terms of age, vitamin B12, HbA1c, LDL-C (p>0.05). Comparison of laboratory data of patients with hypothyroidism and hyperthyroidism in terms of gender is presented in Table 1.

When we compared the hypothyroid and hyperthyroid groups, we found a statistically significant difference between the groups in terms of TSH, fT3, fT4, MPV, PLT, urea, creatinine, LDL-C, TC, TG, and TG/HDL-C ratio. Comparison of laboratory data of the patients in terms by groups is given in Table 2.

When the groups are examined in terms of correlations, in both hypothyroid and hyperthyroid groups, while there was a positive and significant correlation between LDL-C - age, LDL-C - TC, TG - TC, HGB - ferritin, HGB - Fe, HbA1c - TG, AST - ALT, and urea - creatinine, there was a negative significant correlation between HDL-C -TG. Significant correlations of thyroid function tests with biochemistry and hematology laboratory parameters are shown in Table 3. Moreover, vitamin B12 deficiency (B12 levels <175 pg\ml) was present in 8% of hypothyroid patients and 6.3% of hyperthyroid patients. There was no significant correlation between TSH and vitamin B12 and vitamin D.

Table 1. Comparison of laboratory parameters according to gender in patients with hypothyroidism and hyperthyroidism

Hypothyroidism	Female (n: 277)	Male (n: 72)	p value
HGB (g/dL)	14.03± 1.60	15.35 ± 1.93	0.00**
Ferritin (ng/ml)	32.78 ± 32.40	123.50 ± 80.23	0.00**
Vitamin D (ug/L)	13.28 ± 21.12	16.60 ± 5.73	0.08
Vitamin B12 (pg\ml)	283.20 ± 138.20	252.00 ± 104.03	0.10
TSH (IU/L)	6.20 ± 13.31	6.45 ± 12.15	0.69
fT3 (pmol/L)	4.50 ± 1.08	4.75 ± 7.21	0.20
fT4 (pmol/L)	13.50 ± 4.35	14.19 ± 5.21	0.15
TC (mg/dL)	202.00 ± 46.77	189.00 ± 44.13	0.02*
HDL-C (mg/dL)	47.00 ± 12.76	42.10 ± 10.32	0.00**
LDL-C (mg/dL)	119.80 ± 44.65	111.37 ± 36.59	0.16
Hyperthyroidism	**Female (n: 306)**	**Male (n: 72)**	**p value**
HGB (g/dL)	13.75 ± 1.50	15.80 ± 1.54	0.00**
Ferritin (ng/ml)	31.78 ± 32.10	124.40 ± 80.78	0.00**
Vitamin D (ug/L)	9.55 ± 17.31	16.15 ± 10.15	0.01*
Vitamin B12 (pg\ml)	301.00 ± 184.62	291.65 ± 144.03	0.63
TSH (IU/L)	0.29 ± 0.60	0.20 ± 0.48	0.06
fT3 (pmol/L)	5.28 ± 4.42	5.90 ± 5.35	0.00**
fT4 (pmol/L)	16.65 ± 13.42	18.60 ± 18.22	0.01*
TC (mg/dL)	174.00 ± 40.61	165.00 ± 44.40	0.02*
HDL-C (mg/dL)	48.00 ± 13.21	38.00 ± 10.84	0.00**
LDL-C (mg/dL)	99.00 ± 35.01	96.00 ± 37.77	0.14

*p<0.05 **p<0.01, Numerical data are given as mean ± SD

Table 2. Comparison of laboratory parameters in terms of hypothyroidism and hyperthyroidism groups.

Laboratory findings	Hypothyroidism (n: 349)	Hyperthyroidism (n: 378)	p value
Age	46.70 ± 13.97	47.00 ± 14.93	0.16
HGB (g/dL)	14.20± 1.80	14.03 ± 1.68	0.09
Urea (mg/dL)	27.00 ± 17.25	24.80 ± 15.63	0.03*
Creatinine (mg/dL)	0.70 ± 0.56	0.63 ± 0.21	0.00**
HbA1c (%)	6.10 ± 3.12	5.90 ± 1.82	0.81
Fe (mg/dL)	67.28 ± 34.45	75.96 ± 36.37	0.66
Ferritin (ng/ml)	40.20 ± 32.78	44.55 ± 30.23	0.85
Vitamin D (ug/L)	14.07 ± 19.00	11.73 ± 16.45	0.18
Vitamin B12 (pg\ml)	278.10 ± 138.11	298.10 ± 205.48	0.13
TSH (IU/L)	6.28 ± 14.85	0.28 ± 0.60	0.00**
fT3 (pmol/L)	4.50 ± 4.69	5.45 ± 6.91	0.00**
fT4 (pmol/L)	13.80 ± 4.53	17.20 ± 10.09	0.00**
TG (mg/dL)	142.00 ± 99.41	123.00 ± 83.74	0.00**
TC (mg/dL)	199.90 ± 46.51	172.00 ± 41.70	0.00**
HDL-C (mg/dL)	46.00 ± 12.49	46.02 ± 13.39	0.69
LDL-C (mg/dL)	117.19 ± 43.11	98.00 ± 35.64	0.00**
fT3/fT4 ratio	0.34 ± 1.05	0.32 ± 0.48	0.35
TG/HDL-C ratio	4.83 ± 0.57	4.78 ± 0.80	0.00**

*p<0.05 **p<0.01, Numerical data are given as mean ± SD

Table 3. Pearson's correlation coefficients within the patients.

	Correlations	Correlation coefficient (r)	Level	P value
Hypo	TSH - fT4	-0.433	Intermediate	p<0.01
	TSH - fT3/fT4 ratio	0.391	Weak	
	fT3 - HGB	0.350	Weak	
	fT3/fT4 ratio - Vitamin B12	- 0.318	Weak	
	fT4 - Vitamin D	0.274	Weak	
Hyper	TSH - fT4	- 0.490	Intermediate	p<0.01
	TSH- MPV	- 0.355	Weak	
	TSH - Fe	0.274	Weak	
	fT3 – LDL-C	- 0.242	Weak	
	TSH- Age	- 0.238	Weak	

p < 0.05 statistical significance

Discussion

Thyroid hormones are essential for the normal development,

differentiation, metabolic balance and physiological function of all tissues. Both hypothyroidism and hyperthyroidism are more common in females than in males. Our findings in our study are also in this direction [6,11].

Iron deficiency and therefore low ferritin and hemoglobin in women due to reasons such as menstrual cycle and pregnancy are considerably higher than in men. In the findings of our study, we found that HGB, Fe, and ferritin were significantly lower in women in both hypothyroid and hyperthyroid groups compared to men [13].

Mean platelet volume (MPV) indicates mean platelet size and reflects the platelet production rate and stimulation. Some studies have emphasized that there is an increase in MPV in hyperthyroidism and that there is a positive relationship between MPV and TSH [12,14]. Another study on a much larger scale (8424 males, 5198 females) found no association between MPV or PDW and thyroid function [15]. The results of a study in patients with thyroid papillary carcinoma emphasized that MPV is a valuable parameter to monitor the hemostatic status in thyroid disorders [16]. In our study results, we found that the MPV and PLT values were significantly lower in the hyperthyroid group than in the hypothyroid group.

In hypothyroidism and hyperthyroidism, liver and kidney function tests also vary depending on the metabolic rate. In hypothyroidism, renal blood flow decreases, thus affecting the water and electrolyte balance [12,17]. Primary hypothyroidism is associated with reversible elevation of serum creatinine in adults [18]. In a study conducted with 47 overt hypothyroidism, 77 subclinical hypothyroidism and 77 healthy controls, urea and creatinine values were found to be significantly higher in the patient group compared to the control [19]. In our study, urea and creatinine values were significantly higher in the hypothyroid group compared to the hyperthyroid group.

Thyroid hormones increase the utilization of lipid substrates. Hypothyroidism is a well-known cause of hyperlipidemia. The most common lipid abnormality in hypothyroid patients is hypercholesterolemia, mainly due to the increased concentration of LDL-C [10,17,20]. A number of accompanying symptoms of hypothyroidism include hyperlipidemia characterized by up-regulated circulating LDL-C, very TG [21].

A study conducted in 2010 reported that there was a positive correlation between TSH-TC, TSH-HDL-C and TSH-LDL-C in patients with overt hypothyroidism, and a positive correlation between TSH-TC and TSH-LDL-C in patients with subclinical hypothyroidism. In addition, in the same study, it was stated that the TC and LDL-C levels were significantly higher ($p<0.001$) in hypothyroid patients compared to healthy controls, and TC and LDL-C increased as TSH increased [22]. In 2016, the results of studies conducted with 197 hypothyroid, 230 hyperthyroid and 355 healthy controls reported that the TC, TG and LDL-C levels were significantly higher ($p < 0.05$) in hypothyroid patients compared to controls, and the LDL-C and HDL levels were significantly lower in hyperthyroid patients compared to controls ($p < 0.05$) [23]. Another study conducted in 2022 reported that TC, TG and LDL-C levels were significantly higher in hypothyroid patients compared to healthy controls ($p < 0.01$) [24]. TSH had a positive linear correlation with TC ($\rho = 0.277$, $n = 42$, $p = 0.04$).

In this study, a significant increase ($p<0.01$) in serum levels of TG, TC and LDL-C was observed in hypothyroid patients compared to hyperthyroid patients, which is consistent with previous studies. We also found a negative significant correlation between fT3 and LDL-C in patients with hyperthyroidism (r: - 0.238, $p<0.01$).

Limitations of the study

There were some limitations in this study. This study is a retrospective study. In our study, the presence of chronic disease information was obtained from the hospital automation system. There is not enough information about the nutritional habits of the patients and whether they are taking vitamin or mineral supplements. In addition, the absence of a control group in our study is among the limitations of the study.

Conclusion

In this study, a significant increase ($p<0.01$) was observed in TG, TC and LDL-C levels in hypothyroid patients compared to hyperthyroid patients. We also found a negative significant correlation between fT3 and LDL-C in patients with hyperthyroidism (r: - 0.238, $p<0.01$). It is important to understand the effect of thyroid hormones on lipid metabolism. Especially in patients with hypothyroidism, lipid metabolism is highly affected. Our findings emphasize that it is important to follow up both hypothyroid and hyperthyroid patients in terms of lipid parameters.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: *None.*

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:
Ali Fuat Gurbuz, Kamile Yucel. *Effects of hypothyroidism and hyperthyroidism on hematological and biochemical parameters. Ann Clin Anal Med 2023;14(Suppl 1):S10-14*

This study was approved by the Ethics Committee of KTO Karatay University (Date: 2022-05-23, No: 2022/012-05)